SOME EFFECTS OF THE RICE DIET TREATMENT OF KIDNEY DISEASE AND HYPERTENSION*

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KIDNEY cells can be kept "alive" for a few hours in the Warburg apparatus and their chemical reactions examined in a rather simplified set-up.[1] Tissue slices thin enough to permit optimal diffusion are suspended in salt solutions, serum or exudate. The concentration of oxygen, carbon dioxide, sodium bicarbonate, sugar, aminoacids, ketoacids, lactic acid, etc., in the suspension milieu can be quantitatively controlled. Factors such as the rate of arterial and venous blood flow, the lymph flow, and the excretion of urine do not complicate the experiment. From one five-minute period to another one can measure manometrically what these isolated kidney cells do under varying conditions.

Like all other animal tissue, kidney cells have two main sources of energy, oxidation and fermentation. Values of about 10 are given in the literature for BO_2 and QM_{N_2} of human kidney cortex,[2,3] i.e., the approximate amount of oxygen used for oxidative processes by 100 Gm. of fresh kidney substance would be about 5 liters in 24 hours; the approximate amount of lactic acid formed anaerobically in the same time would be about 2 Gm.

If in the course of a disease, renal tissue is destroyed and replaced by a scar, obviously the only metabolic reactions to be found will be those of the scar tissue and no longer those of the kidney cells. Between normal and completely destroyed cells, there are as far as disturbances of cellular metabolism are concerned, the following possibilities:

1. The cells are uninjured, but metabolize in a pathological environment.
2. The cells are injured, but the environment in which they metabolize is normal.

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TABLE I—CHANGES IN CHEMICAL COMPOSITION OF "INFLAMMATION FLUID"

	Serum	*Fluid from Sterile Blister of Skin*
	(*Normal person*)	
Oxygen (mm. Hg.)	110	6
Sugar (mg./100 cc.)	90	6
Lactic Acid (mg./100 cc.)	10	125
Bicarbonate (10^{-3} molar)	25	9
PH	7.4	6.3

3. The cells are injured and metabolize in a pathological environment.

In order to learn something about the chemical composition of such a "pathological environment" we measured the metabolic reactions which take place during an inflammation. We produced sterile cantharidin blisters on the skin of normal people and of patients with various diseases and measured the metabolism of the leukocytes in the blister fluid and the chemical changes produced by them.[4] As Table I shows, the concentration of some biologically essential substances shows a decisive change during inflammation.

The next step was to determine what effects on the metabolism of kidney cells were produced by these environmental changes. We found the anaerobic splitting of sugar into lactic acid to be markedly dependent on changes of the sodium bicarbonate, sugar, and hydrogen ion concentration. The rate of oxidation was, to a large extent, independent of sodium bicarbonate, sugar, and PH, but was dependent on variations of oxygen concentration.

We could show further that the deamination of aminoacids and the formation of ammonia by slices of kidney tissue are inhibited by lowered oxygen concentrations. This applies both to the so-called "unnatural" d-aminoacids and to those naturally present in the plasma of man, rat, and rabbit, and in the tissue slices themselves.[5]

Besides the inhibition of the rate of deamination, which is reversible, there is another effect of low oxygen concentration on kidney cell metabolism which causes irreversible changes. If we kept slices of kidney tissue for about one hour in an oxygen free atmosphere and then re-established conditions of optimal oxygen concentration the cells were still able to deaminize aminoacids and to form ammonia but they had lost the ability to oxidize ketoacids.[6] This means that by the removal of oxygen for a given time one can injure kidney cells selectively as to their oxidative reactions.

The obvious question is: What practical significance have these cellular physiological findings in the treatment of diseases in which renal metabolic dysfunction may play a role. Some simple examples may show the trend of our reasoning. Let us assume that the oxygen *supply* to any one kidney cell has been decreased by some pathological condition and that we are unable to increase it; still, it might be possible to increase the oxygen *concentration* by reducing the amount of work required from this cell, thus decreasing its oxygen demand. Or let us assume that the rate of oxidation of ketoacids in any one diseased kidney cell is decreased; still, it might be possible to reduce the amount of ketoacid offered to the cell if we were able to remove from the diet those substances from which ketoacids are derived. Deductions of a similar kind might be drawn from observation of the role played in renal metabolism by aminoacids, sugar, sodium bicarbonate, etc.

It would be most desirable, of course, to substitute for the natural ferments that have been destroyed, extracts of animal kidneys, or even better, synthetic substances with the same chemical properties as those in normal kidney cells. Unfortunately, such substances are not yet available.

I have been asked to speak to you this evening about a less perfect approach, but one which has led to rather satisfactory results: the compensation of renal metabolic dysfunction with the rice diet.

The consensus of opinion at the present time is that dietary treatment is useful in kidney disease, but of little or no value in hypertension without obvious renal involvement. Goldring and Chasis in 1944 summed up the prevalent view in their book on hypertension: "The diet in uncomplicated hypertension requires no essential change from the normal."[7]

Compared to diets previously used in hypertension, the rice-fruit-sugar diet is rigid. It contains in 2000 calories about 5 Gms. of fat and 20 Gms. of protein derived from rice and fruit, and not more than 0.2 Gm. of chloride and 0.15 Gm. of sodium.[8]

Table II—SERUM CHOLESTEROL OF PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE ON RICE DIET
(Mg. per 100 cc. of serum)

Case	*Before*	*After*	*Days*	*Case*	*Before*	*After*	*Days*
1.	205	178	67	41.	283	205	203
2.	220	191	42	42.	238	210	84
3.	168	175	240	43.	333	270	28
4.	173	170	56	44.	266	154	112
5.	225	177	143	45.	345	258	74
6.	238	200	61	46.	293	200	20
7.	248	200	156	47.	268	170	133
8.	255	215	47	48.	302	217	100
9.	290	150	288	49.	222	70	99
10.	354	275	134	50.	210	190	109
11.	242	172	72	51.	300	225	166
12.	292	237	212	52.	242	152	126
13.	234	173	73	53.	145	188	21
14.	187	186	85	54.	220	166	105
15.	325	226	31	55.	290	160	102
16.	260	192	110	56.	195	168	21
17.	217	190	125	57.	318	235	9
18.	212	176	130	58.	220	187	53
19.	228	166	35	59.	246	220	136
20.	317	186	52	60.	210	205	24
21.	224	155	32	61.	225	200	16
22.	172	160	35	62.	273	230	9
23.	218	135	90	63.	210	143	43
24.	221	192	40	64.	215	155	221
25.	255	146	139	65.	230	153	17
26.	210	225	228	66.	210	175	212
27.	230	164	35	67.	292	168	78
28.	300	198	6	68.	215	110	76
29.	231	213	166	69.	239	149	60
30.	209	181	12	70.	192	215	24
31.	250	247	32	71.	308	246	155
32.	250	260	65	72.	258	175	41
33.	252	161	14	73.	193	153	16
34.	185	108	14	74.	260	170	178
35.	188	150	83	75.	168	160	240
36.	300	203	45	76.	317	170	146
37.	284	235	18	77.	200	175	6
38.	230	228	21	78.	304	169	66
39.	332	246	14	79.	186	102	205
40.	137	175	28				
				Average:	243.2	185.9	

Average Difference 57.3 mg.

It has been argued that this diet is nothing but starvation and that at least the "wear and tear quota" of 45 Gms. of protein is needed to maintain protein equilibrium. This figure, however, has no other basis than the 7 Gms. of nitrogen excreted per day by people who are fasting and represents only the body's effort to meet its caloric requirements by breaking down its own protein. The daily urinary nitrogen excretion of patients who have followed the rice diet for two months or more averages 2.26 Gms., which means that with a daily intake of little more than 15 Gms. of protein due to the protein sparing effect of carbohydrates, the nitrogen equilibrium is maintained.[9] In fasting, the daily urea nitrogen excretion in the urine is about 5.5 Gms. The average daily urea nitrogen excretion in the urine of patients who have followed the rice diet for two months or more is 1.1 Gms.[9]

In fasting, the blood urea nitrogen concentration is higher than it is normally. In patients on the rice diet, the urea nitrogen concentration is below the level of normal (average of 6.6 mg. per 100 cc. of blood). In starvation, hemoglobin and plasma protein concentrations decrease; in patients on the rice diet, the hemoglobin and plasma protein levels are maintained.[9]

It has been argued that the restriction of fat in the rice diet is too rigid and that patients with hypertension should eat "well-balanced meals." On the other hand the relation between hypercholesterolemia and hypertensive vascular disease has been stressed repeatedly, especially with regard to vascular retinopathy, coronary disease, and arteriosclerosis. In a series of 79 patients with hypertensive vascular disease 53 (i.e., 67 per cent) had a cholesterol concentration of at least 220 mg. per 100 cc. serum at the beginning of the treatment. As Table II shows, the hypercholesterolemia decreased with the rice diet in 52 of the 53 patients, the average decrease being 74 mg. per 100 cc. serum; in 37 of these 52 patients, the cholesterol concentration became normal. The hypercholesterolemia increased in 1 of the 53 patients (from 250 to 260 mg.). In 1 patient the cholesterol concentration increased from normal (210 mg.) to a hypercholesterolemic level (225 mg.).

It has been argued that the restriction of salt has no effect on hypertensive vascular disease. Therapeutic results such as those of Allen and Sherrill[10] and of Volhard[11] have been explained by Fishberg[12] on the assumption that salt-poor diets, because of their unpalatability lead to restriction of caloric intake and thus to reduction of the metabolic

Table III—CONCENTRATION (GM.) PER 1000 CC. OF URINE OF PATIENTS ON "NORMAL" DIET AND ON RICE DIET

	Normal Diet	*Rice Diet (after 2 months)*
Urea N	12	1.1
Chloride	6	0.1
Sodium	4	0.01
Potassium	2	3.0
Sodium/Potassium Ratio	2	0.003

rate. According to Page,[13] the effects obtained were due not to salt restriction, but to rest in bed, and the "psychotherapy of constant attention."

With the rigid restriction of sodium and chloride in the rice diet, the sodium and chloride excretion in the urine decreases to minimal amounts. In the urine of patients who have followed the rice diet for one month or longer, the average chloride concentration is about 100 mg., the sodium concentration about 10 mg., the potassium concentration about 3 Gms. per liter, i.e., the potassium concentration is slightly higher than that in the urine of patients on an ordinary diet, the chloride concentration is decreased to about 1/60, the sodium concentration to about 1/400. The sodium-potassium ratio, which in the urine of patients on an ordinary diet is about 2, decreases on the rice diet to 0.003 (Table III).

Grollman and Harrison repeated some experiments with the rice diet, using rats with experimental hypertension; they confirmed our finding, that the rice diet leads to marked blood pressure reduction.[14] Since the hypotensive effect was not obtained when the strict rice diet was changed by the addition of NaCl (not of KCl), this hypotensive effect was ascribed by the authors merely to sodium restriction. Unfortunately, no sodium, potassium, or chloride determinations in blood or urine were made.

No matter which single factor in the rice diet is of greatest importance in compensating the various manifestations of renal metabolic or excretory dysfunction, it remains true that in 203 of 322 patients,

TABLE IV

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White married man. Born 1902. "Always healthy until 1939." Blood pressure checked at two year intervals since 1927. B. P. known to be normal in 1936.

1939 Blood pressure elevated. Treated with Barbiturates.

March 1940 NEW YORK HOSPITAL B.P. 200-165/135-105.
Retrograde pyelograms: "Normal."
"Hypertensive vascular disease."

January 1941 PRESBYTERIAN HOSPITAL, NEUROLOGICAL INSTITUTE
"Hypertensive cardiovascular disease." B. P. 200/140.

February 1941 ROCKEFELLER HOSPITAL B. P. 200/140.
Variations: 196-174/140-120.
"Hypertensive vascular disease; arterial hypertension."
Daily injections of Tyrosinase intravenously for 23 days: Slight decrease in B. P.
Daily injections of Tyrosinase subcutaneously for 13 days: Decrease in B. P. to 150/100.
After one week, B. P. at previous level.

November 1941 B. P. 200/140.
During Tyrosinase treatment: B. P. 164/110.
Because of severe shock-like reaction, Tyrosinase therapy discontinued.

MASSACHUSETTS GENERAL HOSPITAL (Dr. Smithwick):
Lumbodorsal sympathectomy (Dec. 1941-Jan. 1942).

	BLOOD PRESSURE DATA			EKG
	Admission	*Lying*	*Standing*	
Dec. 1941 Before sympathectomy	172/135	180/134	186/145	12-18-41 T_1 upright
Mar. 1944, 26 mos. after sympathectomy	204/144	196/140	150/123	12-29-43 T_1 upright

Beginning 1945 Therapeutical trial with Testosterone: *"Blood pressure higher."*
March 31, 1945: DUKE HOSPITAL Admission 220/132.
(All B. P. readings taken while lying.)
March 31 - April 19, 1945: Average of 20 days in hospital on 1500 cal. reduction diet:
B. P. 197/129.
PSP (total excretion in 2 hours): 62%.
Urea clearance: 125%.
T_1 diphasic. Transverse diameter of heart 14.8 cm.

April 20, 1945: Rice diet started.
Averages:

May 15-21, 1945	129/94	June 1, 1945 full time job resumed.
July 1945	125/90	
August 1945	120/87	
September 1945	126/88	
October 1945	129/87	
November 1945	128/89	
January 8-14, 1946	128/91	T_1 upright. Transverse diameter of heart 13.9 cm.

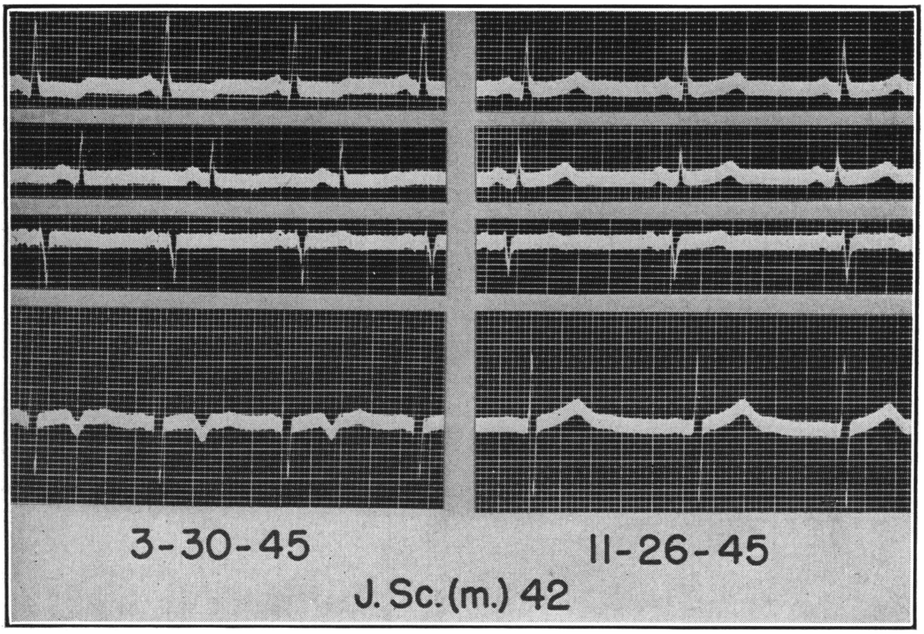

Fig. 1. J.S. (m. 42) "Hypertensive Vascular Disease." Rice diet since 4-20-45. No digitalis. Diphasic T 1 has become upright.

on most of whom other forms of therapy had previously been tried, the rice diet led to objective improvement.

Of 100 patients with primary kidney disease, 65 per cent showed improvement on the rice diet. Of 222 patients where a diagnosis of hypertensive vascular disease was made, 62 per cent improved.

Those who question the value of diet in the treatment of hypertensive vascular disease say that in those patients who responded to the diet our diagnosis was probably incorrect. I think that in most cases the differential diagnosis presents no difficulties. Table IV shows the summary of a typical history.

It would not be right to use such a case as an argument against sympathectomy. I have seen marked blood pressure reduction following sympathectomy, in patients with severe hypertension, and I have seen patients whose blood pressure was not improved. But I do think that the sequence of surgical treatment and dietary treatment should be reversed since the treatment with the rice diet, if it proves to be ineffective, can simply be discontinued.

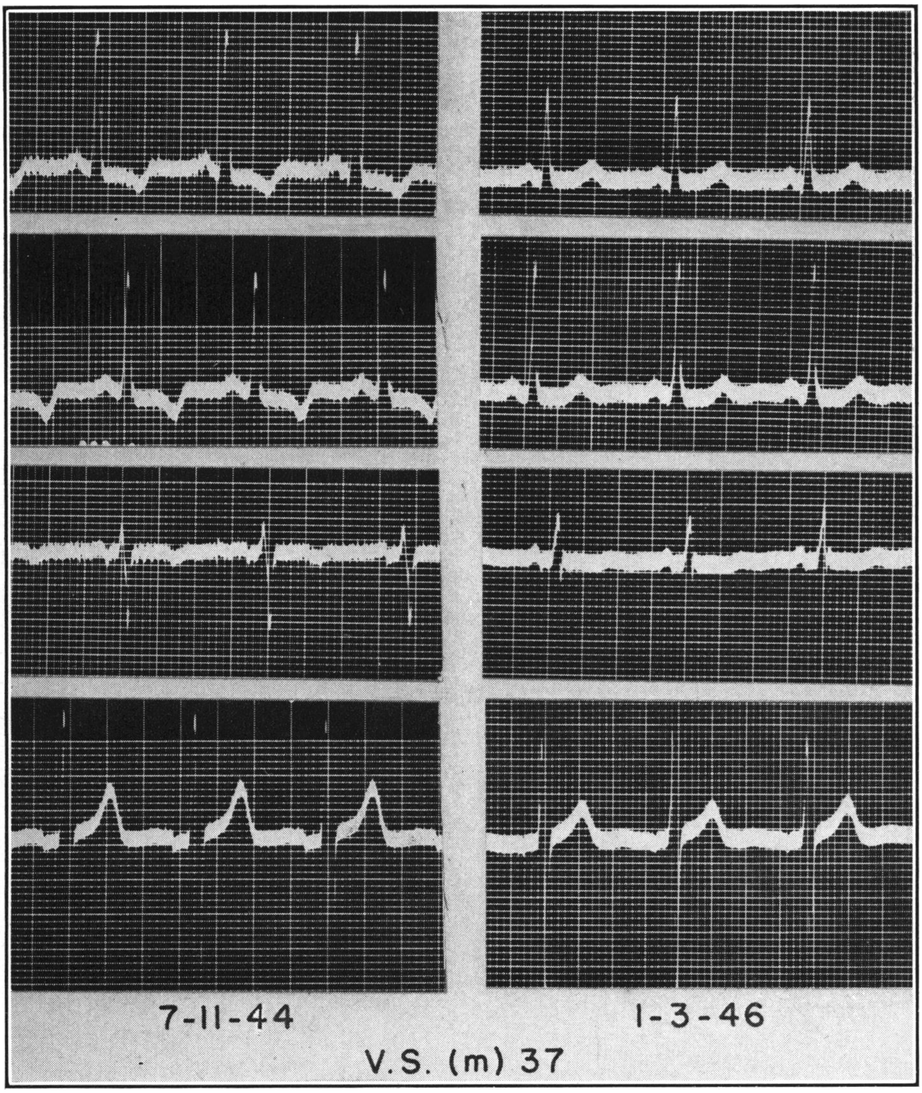

Fig. 2. V.S. (m. 37) "Hypertensive Vascular Disease." Advanced retinopathy. Rice diet since 8-16-44. No digitalis. Change in electrical axis. Inverted T 1 has become upright.

In the patient just mentioned, in spite of the sympathectomy, the electrocardiogram began to show myocardial involvement. T 1 which in December 1941 and December 1943 was upright, had become diphasic by April 1945. With the rice diet, however, the diphasic T 1 reverted to normal (Fig. 1).

We have studied the electrocardiographic changes in 100 patients

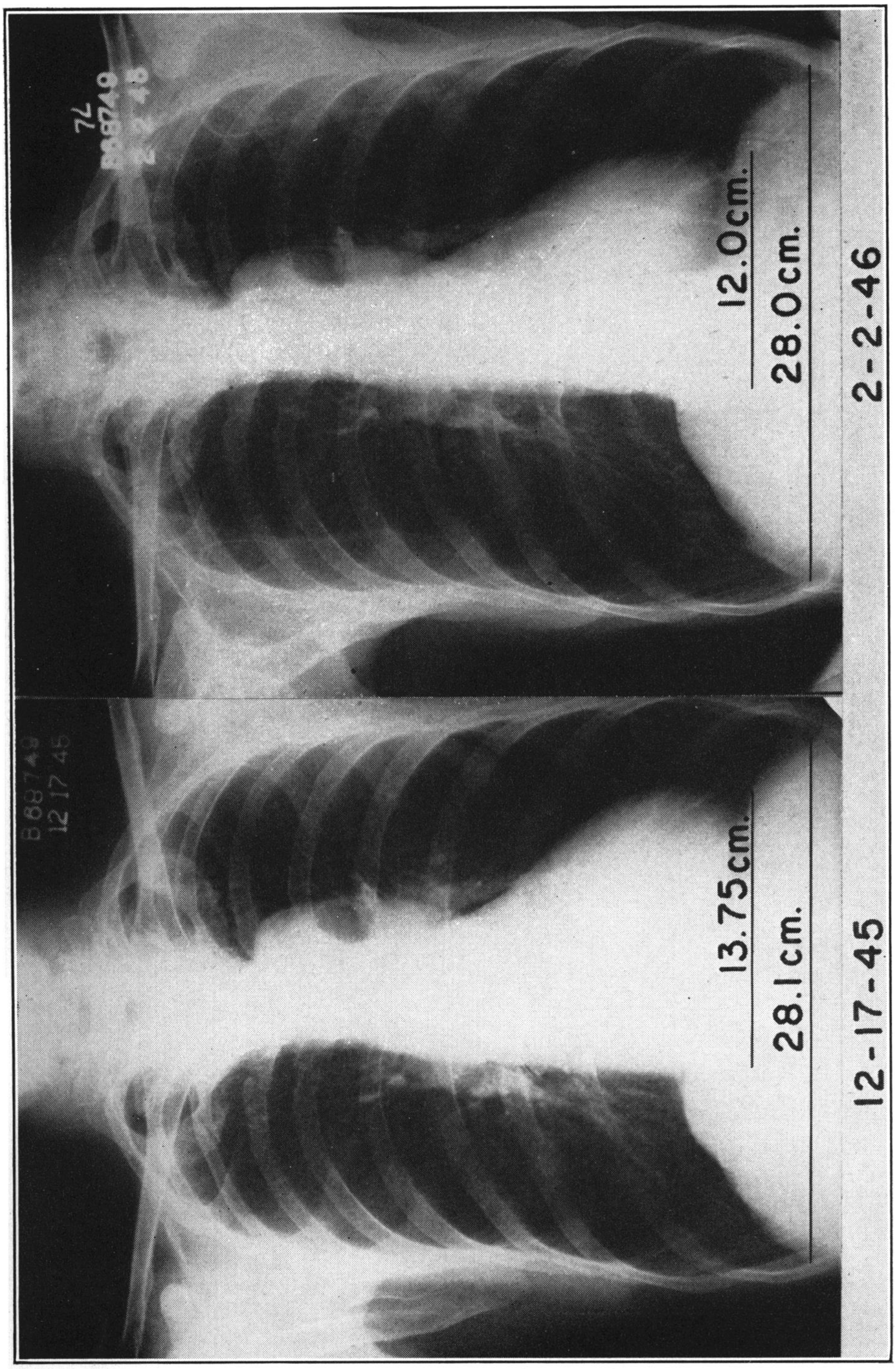

Fig. 3. McD. (m. 62) "Hypertensive Vascular Disease." Rice diet since 1-6-46. No digitalis. Reduction of heart size with change in transverse diameter of 14 per cent.

with hypertensive vascular disease, who have followed the rice diet for two months or longer. In 31 of these patients, the T 1 waves were completely inverted before treatment. In 11 of these 31 patients, T 1 became normally upright with the diet (Fig. 2). In no patient did the reverse occur. The shortest time in which a completely inverted T 1 became upright was two months, the average was six months.

In 77 of 87 patients with hypertensive vascular disease, the heart became smaller in size (Fig. 3). The average change in the transverse diameter was 10.1 per cent. The average chest diameter decreased by less than 0.7 per cent.

In 10 of the 87 patients the heart became larger. In these the transverse diameter of the heart showed an average increase of 2.5 per cent. The average chest diameter increased by 0.54 per cent.

I am sometimes told that enlarged hearts in hypertensive vascular disease become smaller "spontaneously," that electrocardiograms became normal "spontaneously," and that papilledema, hemorrhages, and exudates in the retina disappear "spontaneously."

I have not been fortunate enough to see many of these "spontaneous" recoveries, but I have often seen blindness as a result of advancing vascular retinopathy and death from heart failure, myocardial infarction, renal insufficiency, or cerebral vascular accident in patients who were not willing to submit to any drastic form of treatment because they believed that their disease would clear up spontaneously or that at least it would not become worse.

I have shown you some electrocardiograms and chest films of patients with hypertensive vascular disease who were treated with the rice diet. I will close this talk by showing you a few photographs of eyegrounds (Fig. 4). Forty-four patients with hypertensive vascular disease who had papilledema, hemorrhages or exudates, followed the rice diet for two months or longer. In all of them the retinopathy was arrested. In 20 of the 44 patients papilledema, hemorrhages, or exudates cleared up partially, in 20 completely.

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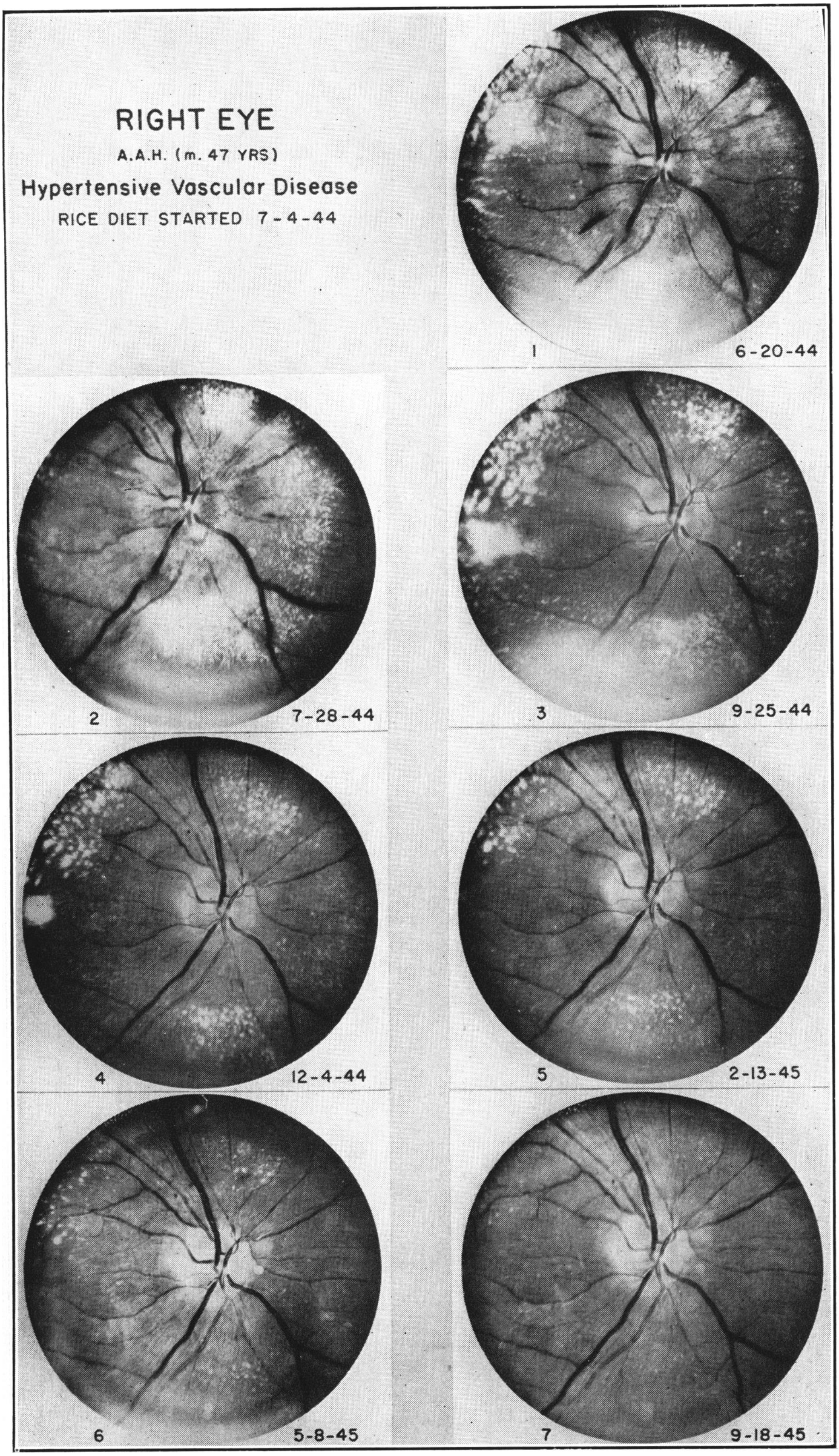

Fig. 4. A.A.H. (m. 47) "Hypertensive Vascular Disease." Rice diet since 7-4-44. *Right eye:* Disappearance of papilledema, hemorrhages, exudates.

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